Propensity matched comparison of extrapleural pneumonectomy and pleurectomy/decortication for mesothelioma patients

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Abstract: OBJECTIVES: The objective of this retrospective study was to assess perioperative outcomes, overall survival and freedom from recurrence after induction chemotherapy followed by extrapleural pneumonectomy (EPP) or pleurectomy/decortication (P/D) in patients with mesothelioma in a propensity score matched analysis. METHODS: Between September 1999 and August 2015, 167 patients received multimodality treatment (platinum-based chemotherapy followed by EPP [n = 141] or P/D [n = 26]). We performed 2:1 propensity score matching for gender, laterality, epithelioid histological subtype and International Mesothelioma Interest Group (iMig) stage (52 EPP and 26 P/D). RESULTS: Postoperative major morbidity (48% vs 58%, P = 0.5) was similar in both groups; however, the complication profile and severity were different and favoured P/D; the 90-day mortality (8% vs 0%, P = 0.3) rate was lower in P/D although not statistically significant. Prolonged air leak (10 days) occurred in 15 patients (58%) undergoing P/D. The intensive care unit stay was significantly longer after EPP (P = 0.001). Freedom from recurrence was similar for both groups (EPP: median 15 months, 95% confidence interval [CI]: 10–21; P/D: 13 months, 95% CI: 11–17) (P = 0.2). Overall survival was significantly longer for patients undergoing P/D (median 32 months, 95% CI: 29–35) compared to EPP (23 months, 95% CI: 21–25) (P = 0.031), but in the P/D group many cases were censored (73%) and the follow-up time was relatively short. CONCLUSIONS: P/D and EPP seem to have similar rates of major morbidity, although the profile of complications is different and more severe after EPP. Freedom from recurrence is comparable in both groups whereas improved overall survival needs to be confirmed in a large patient group with longer follow-up.

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Propensity matched comparison of extrapleural pneumonectomy and pleurectomy/decortication for mesothelioma patients†

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Abstract

OBJECTIVES: The objective of this retrospective study was to assess perioperative outcomes, overall survival and freedom from recurrence after induction chemotherapy followed by extrapleural pneumonectomy (EPP) or pleurectomy/decortication (P/D) in patients with mesothelioma in a propensity score matched analysis.

METHODS: Between September 1999 and August 2015, 167 patients received multimodality treatment (platinum-based chemotherapy followed by EPP [$n = 141$] or P/D [$n = 26$]). We performed 2:1 propensity score matching for gender, laterality, epithelioid histological subtype and International Mesothelioma Interest Group (iMig) stage (52 EPP and 26 P/D).

RESULTS: Postoperative major morbidity (48% vs 58%, $P = 0.5$) was similar in both groups; however, the complication profile and severity were different and favoured P/D; the 90-day mortality (8% vs 0%, $P = 0.3$) rate was lower in P/D although not statistically significant. Prolonged air leak (≥10 days) occurred in 15 patients (58%) undergoing P/D. The intensive care unit stay was significantly longer after EPP ($P = 0.001$). Freedom from recurrence was similar for both groups (EPP: median 15 months, 95% confidence interval [CI]: 10–21; P/D: 13 months, 95% CI: 11–17) ($P = 0.2$). Overall survival was significantly longer for patients undergoing P/D (median 32 months, 95% CI: 29–35) compared to EPP (23 months, 95% CI: 21–25) ($P = 0.031$), but in the P/D group many cases were censored (73%) and the follow-up time was relatively short.

CONCLUSIONS: P/D and EPP seem to have similar rates of major morbidity, although the profile of complications is different and more severe after EPP. Freedom from recurrence is comparable in both groups whereas improved overall survival needs to be confirmed in a large patient group with longer follow-up.

Keywords: Mesothelioma • Extrapleural pneumonectomy • Pleurectomy/decortication • Propensity score matching

INTRODUCTION

Malignant pleural mesothelioma (MPM) is an aggressive neoplasm of the pleura that has a poor prognosis without treatment [1].

Multimodality treatment led to improved overall survival (OS) in mesothelioma patients in past decades [2–5]. However, the exact role and type of surgery remain controversial. Two major types of operations have evolved: extrapleural pneumonectomy (EPP) and pleurectomy/decortication (P/D). EPP is the most radical operation, resecting en bloc both pleural layers, lung, pericardium and diaphragm. P/D is a lung-sparing resection of the pleura and, in selected cases, resection of the pericardium and/or the diaphragm (referred to as extended P/D) [6].

However, the precise role and preferred type of surgery cannot be determined conclusively from the current literature because no randomized clinical trials are available. The International Mesothelioma Interest Group (iMig) group recently concluded that 'based on the current literature and the IASLC (International Association for the Study of Lung Cancer) report, surgery by either P/D or EPP, with the goal of obtaining a macroscopic complete resection (MCR), should be performed in the multimodality treatment of MPM' [7].

The objective of this retrospective study was to assess perioperative outcomes, OS and freedom from recurrence (FFR) after induction chemotherapy followed by EPP or pleurectomy/decortication (P/D) in patients with mesothelioma in a propensity score matched analysis.

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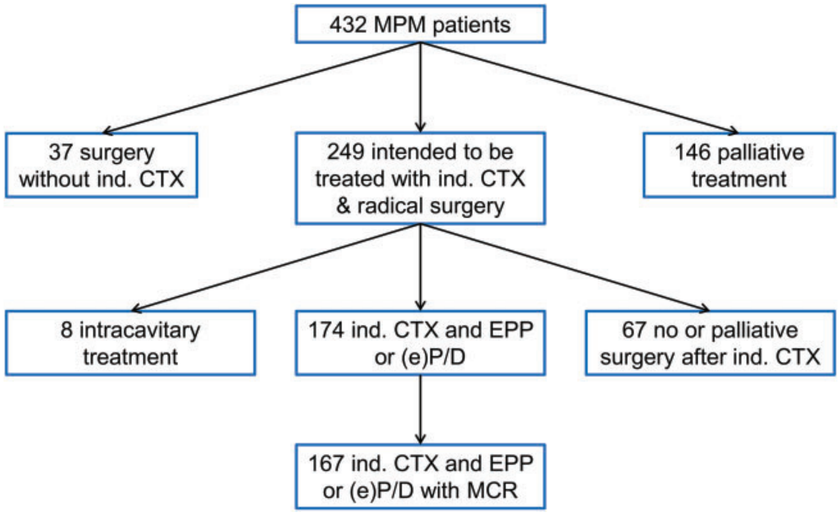

Figure 1: Flow chart of patients with MPM treated at our hospital between September 1999 and August 2015. (e) P/D: (extended) pleurectomy/decortication; EPP: extrapleural pneumonectomy; ind. CTX: induction chemotherapy; MPM: malignant pleural mesothelioma.

MATERIALS AND METHODS

Between September 1999 and August 2015, 432 patients were treated at our hospital (Fig. 1) and 167 patients with the histopathological diagnosis of MPM underwent multimodality treatment consisting of platinum-based induction chemotherapy followed by MCR. Final analysis was performed after propensity score matching in a 2:1 ratio (EPP: $n = 52$ and P/D: $n = 26$). Median follow-up time calculated from the first cycle of chemotherapy was 21 months (range 3–121).

Local ethics committee approval was given for retrospective analysis of the mesothelioma data base (StV 29-2009, EK-ZH 2012-0094).

Multimodality treatment concept

The decision about treatment modalities, including type of surgery, was made by an interdisciplinary tumour board of surgeons, oncologists and radiologists. During the observation period, different neo- and adjuvant protocols were applied; neoadjuvant chemotherapy with cisplatin/pemetrexed was implemented as a standard treatment since the publication of results indicating superior survival rates with this regimen [8] (platinum/gemcitabine: EPP, $n = 20$ [38%]; P/D, $n = 1$ [4%]; platinum/pemetrexed: EPP, $n = 32$ [62%]; P/D, $n = 24$ [92%]). At the time, adjuvant radiotherapy was applied after EPP only in the context of our Swiss multicentre randomized phase III SAKK trial [9]; 29 of 52 patients (56%) undergoing EPP received adjuvant radiotherapy (of these, 6 patients were part of the SAKK 17/04 trial).

Operative technique

EPP and P/D were performed using standard procedures, and MCR was achieved in all cases. The operation and the EPP procedure were performed as described previously [10]. The P/D was done via a lateral thoracotomy in the sixth intercostal space; the parietal pleura was mobilized as a whole towards the hilum; and the visceral pleura was then removed from all lobes including the inter-lobar fissures. For extended P/D, the pericardium and/or the diaphragm were resected depending on extent of tumour infiltration, assessed by intraoperative frozen sections and by the surgeon (two experienced surgeons). Reconstruction was performed using a porcine pericardial patch (Supple Peri-Guard® Pericardium with Apex Processing®, Synovis Surgical Innovations, St. Paul, MN, USA) and Gore Tex patch (Dualmesh® Biomaterial, W.L. Gore & Associates, Inc., Flagstaff, AZ, USA) or Mersilene net (Ethicon Mersilene, Polyester, Johnson & Johnson Intl, New Brunswick, NJ, USA), respectively. Chest wall resection was performed if tumour infiltration was confirmed by frozen section (EPP: $n = 3$; P/D: $n = 1$) and reconstruction was done using a Gore Tex Patch if necessary. After EPP and P/D, all patients were routinely transferred to the intensive care unit (ICU) because of advanced postoperative treatment requirements. One patient who had P/D was monitored postoperatively in the intermediate care unit. The criteria for release from the ICU to the ward included extubation, cardiopulmonary stability and lack of relevant complications.

Statistical analysis

After propensity score matching for gender, laterality, epithelioid histological subtype, and iMig stage in a 2:1 ratio (EPP: $n = 52$; P/D: $n = 26$), perioperative mortality rates (30- and 90-day), postoperative morbidity rates, duration of ICU stay, and duration of hospitalization were determined. Postoperative morbidity was divided into major and minor morbidities; for definitions see Tables 1 and 2.

The Fisher exact test was used for categorical variables and the Mann–Whitney *U*-test, for continuous variables. Numbers are shown as median and range if not otherwise stated. Median OS and median FFR were assessed by Kaplan–Meier curves, and the difference between the two treatment groups was analysed by log rank-test. OS was calculated as the time between application of the first cycle of chemotherapy and death or last follow-up. FFR was calculated as the time between application of the first cycle of chemotherapy and tumour progression. A *P*-value less than 0.05 was considered statistically significant.

All statistical analyses were performed using IBM SPSS Statistics version 22 (IBM Corp., Armonk, NY, USA). Propensity

Table 1: Postoperative mortality and major morbidity

	All EPP ($n = 141$) n (%)	Matched cases EPP ($n = 52$) n (%)	P/D and extended P/D ($n = 26$) n (%)	Fisher exact test (of matched cases)
Mortality				
30-day	7 (5)	1 (2)	0	1.0
90-day	14 (10)	4 (8)	0	0.3
Overall morbidity	131 (93)	48 (92)	20 (77)	0.08
Intraoperative complications	17 (12)	8 (15)	0	0.047
Intraoperative erythrocyte concentrate[a]	37 (39)	14 (44)	9 (35)	0.6
Overall major morbidity	54 (38)	25 (48)	15 (58)	0.5
Prolonged air leak (≥10 days)	0	0	15 (58)	<0.001
Reoperation	50 (36)	23 (44)	7 (27)	0.2
Chylothorax	10 (7)	5 (10)	2 (8)	1.0
Haemorrhage with reoperation	8 (6)	3 (6)	1 (4)	1.0
Diaphragmatic hernia	5 (4)	1 (2)	0	1.0
Patch failure	7 (5)	1 (2)	0	1.0
Empyema	32 (23)	16 (30)	1 (4)	0.008
Early	10 (7)	4 (8)	1 (4)	0.7
Late (>1 month)	23 (16)	12 (23)	0	0.003
Bronchopleural fistula	17 (12)	12 (23)	0	0.007
Pulmonary embolism	4 (3)	1 (2)	0	1.0
ARDS	2 (1)	1 (2)	1 (4)	1.0
Tracheotomy	5 (4)	1 (2)	1 (4)	1.0
SIRS	5 (4)	0	3 (12)	0.04

[a]Information was not available for all patients.

ARDS: acute respiratory distress syndrome; EPP: extrapleural pneumonectomy; P/D: pleurectomy/decortication; SIRS: systemic inflammatory response syndrome.

Table 2: Postoperative minor morbidity

	All EPP ($n = 141$) n (%)	Matched cases EPP ($n = 52$) n (%)	P/D and extended P/D ($n = 26$) n (%)	Fisher exact test (P-value)
Transfusion	63 (45)	21 (40)	16 (62)	0.1
Seroma	35 (25)	14 (27)	0	0.003
Horner syndrome	11 (8)	3 (6)	0	0.5
Recurrent nerve palsy	7 (5)	1 (2)	1 (4)	1.0
Pneumothorax (requiring drainage)	0	0	2 (8)	0.1
Pleural effusion (requiring drainage)	37 (26)	10 (19)	2 (8)	0.3
Pericardial effusion	1 (1)	0	1 (4)	0.3
Mediastinal shift (requiring intervention)	41 (29)	17 (33)	0	<0.001
Atrial fibrillation (requiring medication)	50 (36)	16 (31)	4 (15)	0.2
Deep vein thrombosis	1 (1)	0	1 (4)	0.3
Angina pectoris	1 (1)	1 (2)	0	1.0
Pneumonia	5 (4)	0	1 (4)	0.3

EPP: extrapleural pneumonectomy; P/D: pleurectomy/decortication.

score matching was performed on a logit scale with a calliper of 0.2 using the package Matching in R (R Development Core Team).

RESULTS

The EPP and P/D groups were matched using a 2:1 propensity score-based matching process. A total of 52 patients from the EPP and 26 patients from the P/D group (15 extended P/D, 11 P/D) were available for analysis. Patient's characteristics did not differ significantly; however, patients undergoing EPP were significantly younger than patients undergoing P/D (Table 3).

Patients undergoing EPP or P/D had comparable major postoperative morbidities (48% vs 58%, Fisher exact test $P = 0.5$) (see Table 1). Major morbidities for the EPP group were empyema (30%), bronchopleural fistula (BPF) (23%), chylothorax (10%) and patch failure (2%) whereas prolonged air leak (≥10 days) accounted for most major morbidities in the P/D group and was present in 15 patients (58%) (Table 1). Median time until chest tube removal in patients with prolonged air leak was 22 days (range: 10–34). Empyema developed in 1 patient after P/D (4%), presenting with a concomitant prolonged air leak (25 days).

Table 3: Patient characteristics

	All EPP (n = 141)	Matched cases EPP (n = 52)	P/D and extended P/D (n = 26)	Fisher exact test (P-value)
Male, n (%)	125 (89)	51 (98)	25 (96)	1.0
Right-sided MPM, n (%)	77 (55)	35 (67)	18 (69)	1.0
Epithelioid histological characteristics, n (%)	90 (64)	49 (94)	24 (94)	1.0
iMig pathological stage, n (%)				
I	11 (8)	5 (10)	2 (8)	1.0
II	29 (21)	13 (25)	7 (27)	
III	85 (60)	30 (58)	15 (58)	
IV	16 (11)	4 (7)	2 (7)	
				Mann–Whitney U-test (P-value)
Age at surgery, years	61 (36–73)	61 (38–72)	66 (34–77)	0.003

EPP: extrapleural pneumonectomy; iMig: International Mesothelioma Interest Group; MPM: malignant pleural mesothelioma; P/D: pleurectomy/decortication.

Table 4: Surgery and hospitalization

	All EPP (n = 141)	Matched cases EPP (n = 52)	P/D and extended P/D (n = 26)	Fisher exact test, P-value
Intraoperative complication, n (%)	17 (12)	8 (15)	0	0.047
Reoperation, n (%)	50 (36)	23 (44)	7 (27)	0.2
				Mann–Whitney U-test (P-value)
Surgery duration, min	360 (230–630)	360 (270–580)	460 (235–635)	0.006
Blood loss, ml	700 (150–4000)	800 (150–4000)	900 (200–3500)	1.0
Reoperation, n	0 (0–14)	0 (0–14)	0 (0–4)	0.07
ICU, days	3 (1–97)	3 (1–21)	2 (0–19)	0.001
Postoperative hospital stay, days	14 (4–131)	14 (7–38)	15 (7–106)	0.4

EPP: extrapleural pneumonectomy; ICU: intensive care unit; P/D: pleurectomy/decortication.

Empyema after EPP was associated primarily with BPF (12 patients) but also presented without BPF (4 patients). Late empyema after EPP (>30 days) was observed more often than early empyema (12 vs 4 patients). Reoperation was performed more often after EPP (44% vs 27%, P = 0.2; see Table 4). Indications for reoperation included empyema, BPF, chylothorax, patch failure and haemothorax in patients who had EPP whereas the sole indication for reoperation in patients after P/D was empyema. All patients with empyema underwent accelerated empyema treatment [11] with repetitive debridement and placement of a muscle or omental flap; open-window thoracostomy was avoided in all cases. A pulmonary embolism that occurred 46 days after discharge from the hospital was the cause of death of 1 patient treated with EPP. Pneumonia was observed in 1 patient after P/D, and acute respiratory distress syndrome was observed in 1 patient from each group. The postoperative ICU stay was significantly longer for patients who had EPP (3 days [1–21] vs 2 days [0–19], P = 0.001; see Table 4). For minor morbidities, see Table 2.

The 30-day mortality rate was similar in both groups (2% vs 0%, P = 1.0) (Table 1) whereas the 90-day mortality rate tended to be higher in patients who had EPP (8% vs 0%, P = 0.3). Causes of death up to 90 days postsurgery included septic multiorgan failure (EPP, Day 63), pulmonary embolism (EPP, Day 46), cardiogenic shock (EPP, Day 20) and tumour progression (EPP, Day 85).

Long-term oncological outcomes

FFR was comparable for both groups, although lower in the EPP group (EPP: median 15 months; 95% CI: 10–21 months; P/D: median 13 months; 95% CI: 11–17 months) (P = 0.3). OS seemed to be longer for patients undergoing P/D compared to those having EPP (P/D: median 32 months; 95% CI: 29–35 months vs EPP: median 23 months; 95% CI: 21–25 months; P = 0.03). However, 19 patients (73%) were censored (Fig. 2).

DISCUSSION

Although rates of morbidity were similar between the EPP and P/D groups in this propensity score matched analysis, severity and profile of complications were different. Moreover, long-term oncological outcome was difficult to interpret because many patients were censored, previous data were confirmed [12], and FFR may be shorter after P/D whereas OS seems to be comparable with both techniques. In the absence of randomized data, we applied this study concept using a propensity score-based matching for iMig stage as well as for other known prognostic factors (gender, histological subtype [1] and laterality of the disease [13]).

The long-lasting debate on the role of each of the two techniques cannot be answered definitely from the current literature,

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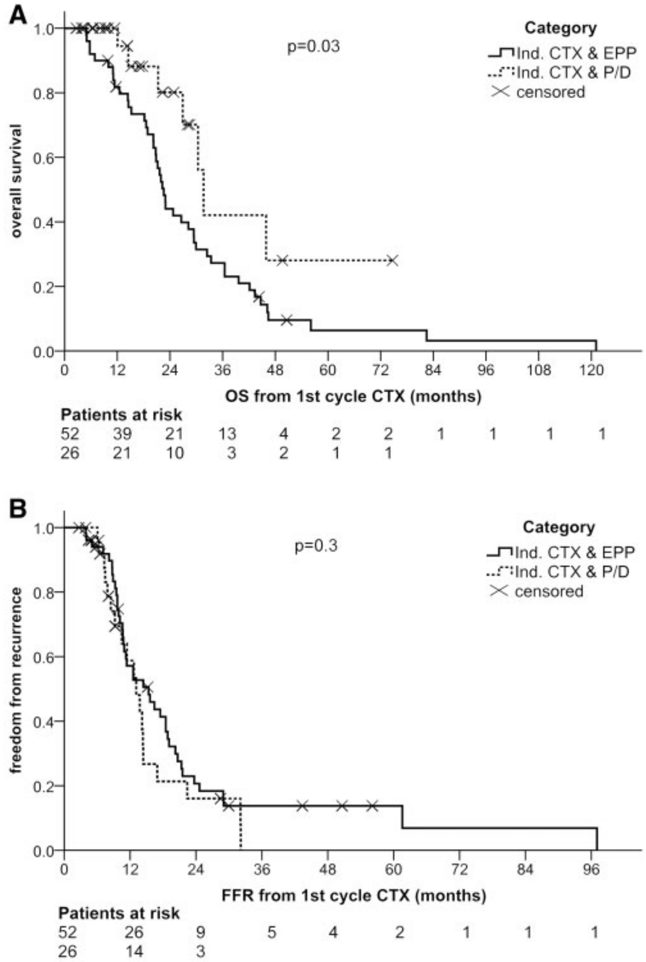

Figure 2: Kaplan–Meier survival curves comparing both treatment groups. Treatment groups were matched for gender, laterality, International Mesothelioma Interest Group (iMig) pathological stage and histological subtype (2:1 ratio). (**A**) Significant difference in OS between patients treated with EPP ($n = 52$) (median OS: 23 months; 95% CI: 21–25 months) and patients treated with P/D ($n = 26$) (median OS: 32 months; 95% CI: 29–35 months), $P = 0.03$. (**B**) No significant difference in FFR between patients treated with EPP ($n = 52$) (median FFR: 15 months; 95% CI: 10–21 months) and patients treated with P/D ($n = 26$) (median FFR: 13 months; 95% CI: 10–17 months). CI: confidence interval; EPP: extrapleural pneumonectomy; FFR: freedom from recurrence; OS: overall survival; P/D: pleurectomy/decortication.

because the available data are significantly heterogeneous and inconsistent [12–14]. The different treatment algorithms used and the different experience levels of the centres involved as well as the inconsistency of nomenclature and definitions are the main problems; the latter has been addressed recently, and uniform definitions have been suggested for P/D [6]. Furthermore, the heterogeneity of the disease itself, especially the unpredictable biological behaviour, cannot be considered in these studies. In the largest meta-analysis, which included 24 studies with 1512 patients after P/D and 1391 patients after EPP, just over half of the studies (53%) favoured EPP in terms of oncological outcomes whereas 47% favoured P/D [12]. A different meta-analysis including 7 more congruent studies with 632 and 513 patients for EPP and P/D, respectively, concluded that P/D seems to have similar, if not superior, long-term survival rates [15]. Data on postoperative morbidity and short-term mortality, however, favour P/D, showing more postoperative complications and significantly higher 30-day mortality rates after EPP [12, 15]. Nonetheless, the data on mortality and morbidity remain extremely heterogeneous due to differences in the patient cohorts and in definitions of morbidity.

According to our results, both procedures appear to have similar rates of major morbidity: the rates of 48% and 58% for EPP and P/D in experienced centres are comparable to published data ranging from 10% to 82.6% and 5.9% to 55%, respectively [14]. Each operation has its specific set of possible and frequent complications that derive from the actual principles of each operation and are therefore not directly comparable, whereas after EPP, complications can quickly become life threatening. Whereas BPF exists only after EPP, prolonged air leak can only occur after P/D; empyema derived from BPF in most cases, but also occurred without BPF in 4 patients undergoing EPP and in 1 patient having undergone P/D, which, in this case, might be triggered by a prolonged air leak with ascending infection via the chest drains. Our rate of empyema after EPP, which is higher than that reported in the literature, may be improved by prophylactic coverage of the bronchial stump with viable tissue. Reoperations were performed more frequently after EPP for indications such as empyema, BPF, chylothorax, patch failure and severe haemorrhage whereas reoperation for the closure of a prolonged air leak was never necessary. A prolonged air-leak, however, was present more frequently in our series (58%) than in series from previously published studies, ranging from 13.5% to 33.3% [16–18]. This large discrepancy may derive from heterogeneous definitions and even more so from a not yet standardized procedure with different extents of decortication or the fact that some groups do not count prolonged air-leak as a major morbidity. Our own experience shows that rigorous decortication that includes the whole surface of the lung as well as the interlobar fissures, even if no macroscopic tumour is observed, is important, because fresh-frozen sections taken during the operation confirmed the presence of tumour in these parts of the pleura.

Our results concerning perioperative deaths compare extremely favourably with those in the published literature; we observed a 2% 30-day mortality rate after EPP and zero 30-day deaths after P/D compared with data from a systematic review reporting 3.2%–12.5% and 0%–9.8% 30-day mortality rates for EPP and P/D, respectively [14]. However, 90-day mortality data have been shown to be a better estimate for the risk of a thoracic operation [19]; recent data from the UK show a 13.5% 90-day mortality rate for EPP and 9.2% mortality rate for P/D [18]. Our results were strikingly low, with 8.0% and 0.0% 90-day mortality rates for EPP and P/D, respectively, even though they were not significantly higher after EPP. The low 90-day mortality rate on the one hand and the high rate of empyema in the EPP group on the other hand may partially be explained by the good outcomes of our accelerated empyema treatment concept; in other words, patients who might have died of empyema in other centres may survive in our centre because of this treatment option [11].

Long-term survival seemed to be better after P/D in our study: FFR after P/D (13 months, 95% CI: 10–16) was similar to FFR after EPP (15 months, 95% CI: 10–21); OS, however, tended to be longer in patients having undergone P/D (32 months 95% CI: 29–35) compared to patients having undergone EPP (23 months, 95% CI: 21–25). As described previously, the paradoxical behaviour of better OS despite earlier local recurrence may be multifactorial and may derive from a lower operative mortality rate for P/D but especially also from a better tolerability of disease progression needing further treatment when both lungs are in place; this argument is, however, purely hypothetical. Moreover, these results have to be viewed critically because of the small sample size and the many censored cases in the P/D group.

A quality of life assessment is not available for all patients included in this study; therefore no definitive statements about the effect of each procedure on quality of life can be made. However, it has previously been suggested that quality of life may be less affected by P/D than by EPP [17, 20, 21]. We agree that a prolonged air leak might have a lesser impact on quality of life than empyema, BPF and the need for reoperation.

The role of surgery as part of the multimodality concept has been debated heavily since the results of the MARS trial were published [22]. However, the underpowered design and the high-postoperative mortality rates made these results questionable [23]. We could not address the role of surgery itself in this study, because no un-operated group from our database could be matched for iMig stage. However, with a median OS of 22 and 32 months for EPP and P/D, respectively, both techniques seem to be at least as good as chemotherapy only with a median OS of 19.5 months published in the MARS trial [22].

We are aware of several limitations of this study. First, the protocol of the neoadjuvant chemotherapy regimen changed over time, which might have an impact on survival. More patients undergoing EPP received platinum/gemcitabine compared to platinum/pemetrexed in the P/D group. Because it has been suggested that adding pemetrexed to platinum-based chemotherapy regimens increases median survival as well as response rates [8], patients who had P/D may have had a survival benefit. However, our data show no difference in long-term survival of patients receiving platinum/pemetrexed compared to those receiving platinum/gemcitabine (21 months [95% CI: 15–26] with cisplatin/gemcitabine versus 18 months [95% CI: 12–24] with cisplatin/pemetrexed [$P = 0.8$]) [24]. In the present study, none of the patients undergoing P/D had radiotherapy for technical reasons while 56% of patients who had EPP received additional radiation therapy, some as part of the SAKK 17/04 study, which did not show a benefit for prophylactic hemithoracic radiotherapy [9]. The fact that the direct effects of these different treatment modalities on overall survival cannot possibly be evaluated properly limits the impact of our results concerning long-term oncological outcomes.

Second, the retrospective design might have added some selection bias that we could eliminate to a certain extent by propensity score matching. Older age has previously been described as a prognostic factor but could not be included in our propensity matching process. However, postoperative mortality and long-term outcomes were worse in patients undergoing EPP, which represented the younger group.

Third, the limited numbers and many censored patients in the P/D group may affect the significance of our long-term oncological outcomes. Moreover, because all of the P/Ds have been performed in recent years and with less frequency, there might have been a general learning curve effect for the management of MPM patients in general and a learning curve for the P/D procedure in favour of EPP. However, the treatment algorithms have not changed substantially at our centre over the last several decades.

Larger studies are needed to further elucidate the best surgical treatment and to determine the right indications for each procedure. To optimal decision making, it is crucial to involve an interdisciplinary tumour board with experienced mesothelioma surgeons at a dedicated, high-volume mesothelioma centre and to tailor an individual treatment plan for each patient. We further believe that an algorithm has to be established within the guidelines to decide on the type of treatment. The Multimodality Prognostic Score, an algorithm suggested by our group, has shown good risk stratification for survival after EPP, taking into account tumour volume, histological subtype, preoperative c-reactive protein levels and tumour response according to RECIST criteria [24]. In the future, these tools will be further refined to better prepare the clinician to choose a treatment strategy on the basis of individual risks and potential benefits for each patient.

Both surgical techniques appear to be feasible after induction chemotherapy and may lead to improved long-term survival compared to chemotherapy alone in carefully selected patients. Although the rates of severe complications and 90-day deaths are higher (but not significantly) after EPP, the overall morbidity rates seem to be equal in the present data set. Each procedure is characterized by its own specific set and severity of complications and represents different challenges for perioperative management. There is a tendency to preserve EPP for selected cases only as long as P/D can achieve an MCR and the remaining lung will be of relevant size and quality. Each procedure will have specific indications that need to be further refined in future trials.

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